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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,436	10/27/2003	Kathleen C.M. Campbell	STU 7397	8942

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EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
06/27/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@senniger.com

Office Action Summary	Application No.	Applicant(s)	
	10/694,436	CAMPBELL, KATHLEEN C.M.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/14/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-20,22-32 and 38-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-20, 22-32 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/14/08; 6/20/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 5/14/08 and 6/20/08 have been reviewed.

Status of claims

Claims 1, 3-20, 22-32 and 38-40 are pending. Claims 38-40 are newly applied.

Response to Arguments

The response filed 5/14/08 has been received and entered. The text of those sections of Title 35 U.S. Code not included in this action can be found in the prior Office action. Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

Claims 10-15, 18-19, 26-28 and 30-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn, Applicant amended the claims and no longer contain the rejected terms.

Claim Rejections - 35 USC § 103

Claims **1 and 3-20 and 22-37** rejected under 35 U.S.C. 103(a) as being unpatentable over Neuwelt, 2004/0198841 A1 is withdrawn because Applicant showed through 131 declaration filed that the application was diligently reduced to practice prior to the priority date of Neuwelt.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7-9, 20 and 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Gabrilove, US 4,961,926.

The reference discloses a method of treating oral mucositis in a human patient resulting from radiation, wherein the compound administered is a non-glycosylated polypeptide having an amino acid sequence identical to the sequence of the polypeptide stimulating factor wherein there is a methionine at the end-terminus. It is interpreted that the administering a protective agent comprising can include not only methionine. Therefore the art teaches the claimed invention of instant claims 1 and 20. See col. 4, lines 25-30 and 35-37 and col. 8, lines 60-65. With regard to the protective agent administered prior to radiation, simultaneously and or subsequently as required by instant claims 7-9 and 23-25, see col. 4, lines 38-42. Mucositis is defined in the art as

oral mucosa see, col.1, lines 57-60. Administering the drug will inherently reduce oral mucositis, as disclosed, see col. 4, lines 55-58.

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3-9, 10-19, 22 and 26-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell US 6,187,817 in view of Gabrilove, US 4,961,926 further in view of Kil et al., WO 03/045334 (same as 2003/0157191 taken from Applicants IDS).

Campbell teaches reducing gastrointestinal toxicity, administering D-methionine, wherein the protective agent is D-methionine as required by instant claims 3-4 and 22- see abstract and col. 1, lines 20. The reference teaches administering a supplemental amount, orally wherein administration of methionine should be designed to achieve the serum levels equivalent to those achieved via parenterally doses from 1.0 mg-500 mg/kg body weight. See col. 17, lines 36-47, col. 17, lines 30-56 and col. 24, lines 59-65 (claims 13-17, 29-30). The reference also discloses the protective agent is administered from 6 hours before to 6 hours after exposure to chemotherapeutic agent, within 1 hour before and 1 hour after chemotherapeutic agent and one –half hour before and after chemotherapeutic agent as required by instant claims 13-15. Obviously the

blood serum level will comprise a blood serum level of at least 10%- 70 % because if the same effective amount is administered, the blood serum level is expected to be the same as required by instant claims 18-19, 27-29, and 31-32.

With regards to claim 6, the reference teaches methionine is substantially free of the L-isomer, since it is substantially free it does not disclose methionine absolutely free of the L-form therefore interpreted as if containing some fraction of L-isomer.

The reference fails to teach (i) reducing mucositis, (ii) administration of methionine to a patient in the time period recited in instant claims 10-12 and also (iii) methionine as L-methionine.

Gabrilove is applied here as above.

Kil et al. teach administering methionine and DL- methionine to patients for the ameliorating undesirable effect of chemotherapy. See page 1 para. 0003-0006 and 0008.

One of ordinary skill in the art would have been obvious to one of ordinary skill in the art to administer substitute the compound of Gabrilove and administer D-methionine because the reference teaches D –methionine is used for neurotocicity. As evidence by Rapoport et al (J. Clin. Oncol. 17; 2446-2453 1999) in the conclusion statement disclose gastrointestinal toxicity is a major cause of transplant-related morbidity and mortality, emphasizing the need for corrective strategies. The peak oral mucositis score and the duration of parenteral nutritional support are useful indices of gastrointestinal toxicity because these end points are correlated with clinically significant events, including blood infections and treatment-related mortality. Therefore administering methionine for the

treatment of gastrointestinal toxicity would have reduced oral mucositis because gastrointestinal toxicity is closely related to oral mucositis as explained and also as shown high dose of chemotherapy and radiation induce changes in the mucosal and gastrointestinal tract. See lft. col. page 2446 underlining.

It would have been obvious to administer radiation prior to or simultaneous or subsequently to the patient receiving the protective agent methionine because the Gabrilove teaches chemotherapeutic agents and or radiation can administered in that manner. Therefore would have been obvious to administer radiation in the manner recited in the claim because it has been taught in the prior art.

It would have been obvious to one of ordinary skill in the art to use any form of methionine for the treatment of mucositis because even though Kil disclose the use of either methionine (which can be either in its D or L or a mixture of DL-forms as interpreted by the Examiner) for ameliorating side effects caused by chemotherapeutic agents, it is known in the that oral mucositis is a common effect of chemotherapy. See as evidence by Rossenbaun et al. (Cancer Supportive Care Programs) underlining sec. One of ordinary skill in the art would have expected any form of methionine would have worked in the treatment of oral mucositis.

Claims 38--40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell US 6,187,817 in view of Gabrilove, US 4,961,926 (applicants IDS) and further in view of Kil et al., WO 03/045334 (same as 2003/0157191).

Campbell and Gabrilove are applied here below as above.

Further Campbell teaches the patient is undergoing treatment with chemotherapeutic effective anti-tumor platinum coordination compound, wherein the platinum compound is cisplatin. See col. 23, lines 63-67 and col. 25, lines 31-33.

Kil et al. teach administering methionine and DL- methionine to patients for the ameliorating undesirable effect from chemotherapeutic agents. See page 1 para. 0003-0006 and 0008.

It would have been obvious to one of ordinary skill in the art to use methionine in a patient undergoing treatment with a platinum containing chemotherapeutic agent because as taught by Kil, methionine is administered to set population for the amelioration of the undesirable side effects from the chemotherapeutic agents.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/SVG/
6/16/08